late systolic extrasounds. The abnormalities consist of T-wave flattening and inversion in leads II, III, avf, V_{4-6}. Evidence of transmural myocardial infarction is seen rarely. Exercise electrocardiograms in patients with chest pain and auscultatory evidence of floppy valves are frequently positive exhibiting ST segment depression despite normal coronary arteriograms. Exercise testing may precipitate arrhythmias, including multiple premature ventricular contractions and ventricular tachycardia. Thus, such tests in patients with the ballooning mitral valve syndrome should be performed with caution and careful monitoring.

Diagnostic Studies

A number of noninvasive tests may be used to establish the origin of the late systolic murmur as mitral regurgitation. Amyl nitrite administration causes the mid-late systolic extrasound to move earlier in systole frequently merging with the first heart sound. The late systolic murmur also moves earlier in systole and may become pansystolic; its intensity does not change.

Handgrip may be very effective in evaluating these auscultatory phenomena. Handgrip may bring out a systolic extrasound which is evanescent and difficult to document.

Ultrasound examination of the mitral valve often is characteristic in the syndrome. Abnormal motion of the anterior leaflet as well as clear separation of the leaflets on the echogram are common. When present, these signs are nearly pathognomic of the ballooning posterior leaflet syndrome.

A majority of patients with either midsystolic extrasounds or late systolic murmurs are asymptomatic. Their prognosis for longevity appears independent of the extent of abnormality in the mitral leaflets. However, the occurrence of chest pain and arrhythmias is associated with considerable prognostic uncertainty. The rate of progression of the mitral regurgitation is unknown. Thus, asymptomatic patients with the auscultatory phenomena of the syndrome must be followed periodically.

When chest pain is prominent, treatment with propranolol and long-acting nitrates may be initiated. This mode of therapy has afforded significant relief in some patients. Control of arrhythmias is indicated in light of the incidence of sudden death. Ventricular extra systoles should be treated with propranolol and digitalis, while atrial arrhythmias can often be managed effectively with digitalis alone.

CLINICAL CARDIOLOGY SERIES

Treatment of Cardiogenic Shock

Part 1

LAWRENCE S. COHEN, M.D.

Material Supplied by the American Heart Association

ALTHOUGH THE TREATMENT of cardiac arrythmias following a myocardial infarction has decreased in-hospital mortality, cardiogenic shock remains a major cause of death. The mortality rate of cardiogenic shock is still in the range of 75 to 80 percent. It is estimated that more than 100,000 persons die yearly in the United States with this syndrome. The clinical profile of the patient with cardiogenic shock is familiar. At some point after a heart attack the blood pressure starts to fall and is usually no greater than 80 mm of mercury systolic. Tachycardia, 120 to 140 beats per minute, is quite usual. The skin color is a dusky cyanotic gray and the patient is markedly diaphoretic. Urine output falls and the patient's sensorium becomes clouded. He will often be barely arousable or may be quite irrational. Terminally, ventricular tachyarrhythmias or heart block may occur.

If any one form of therapy had proved to be successful there would be little controversy concerning the proper medical therapy for this condition. Since the mortality is so high, many forms of therapy have been advocated. In the absence of uniform agreement concerning therapy the following approach is one which the author accepts as a generally reasonable one. It

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Dr. Cohen is from Yale University School of Medicine, New Haven.

is axiomatic that therapy must be individualized for each patient and that no patient should receive a predetermined regimen.

The principles of therapy for cardiogenic shock follow from the pathophysiology of this condition. There is increasing evidence that the major factor leading to cardiogenic shock is an inability of the left ventricle to perform adequately as an effective pump. In almost all cases cardiac output is markedly diminished. Similarly, the hypotension which is a hallmark of this syndrome is in large part a consequence of low cardiac output. Since a critical pressure is necessary to maintain coronary filling, the hypotension has deleterious effects upon coronary filling and this in turn leads to further deterioration in the ability of the heart to support the circulation.

The two goals of therapy for this condition are (1) to increase the cardiac output and (2) to raise systemic blood pressure. Both of these goals could be achieved if the left ventricle were helped sufficiently to augment its contractility.

General Considerations

Since cardiogenic shock has such a dreadful prognosis, any patient with this syndrome should be treated in a specialized facility capable of handling the intricate problems that arise. Adequate bedside and central nursing station electrocardiographic monitoring should be available. An intravenous line capable of measuring central venous pressure should be present and fluids and medication may be administered through it. Although it is desirable in certain circumstances to be able to directly record arterial pressure through the use of a strain gauge and pressure transducer, this latter intervention is not absolutely essential.

The measurement of central venous pressure may be important in unmasking hypovolemia as a contributory factor to the shock. With the widespread use of diuretics in cardiac patients it is not unusual for the patient who sustains a myocardial infarction to have the problems of hypovolemia added to those of pump failure. Although it is well recognized that the central venous pressure may be totally normal, even if the patient is in pulmonary edema, knowledge of the central venous pressure does help management. If the central venous pressure is low or normal and if the patient is not in gross left sided congestive heart failure with rales, dyspnea and roentgenographic evidence of pulmonary edema, judicious fluid therapy may be extremely valuable in reversing the state of circulatory failure. By taking advantage of the fact that as left ventricular end diastolic pressure and volume increase, so will left ventricular work and stroke output, a trial of 250 ml of isotonic saline solution or low molecular weight dextran may be tried. If this improves the circulatory state, then another 250 ml may be given. At times a simple therapeutic maneuver such as fluid administration may be of great help in relieving many of the manifestations of this syndrome.

If central venous pressure is elevated in the absence of cor pulmonale, there is generally little chance that fluid administration will be helpful and the danger of causing pulmonary edema increases.

Other general principles such as oxygen administration and adequate pain relief will not be commented upon here, other than to mention them. Pain, such as that which may occur with a myocardial infarction, may often lead to vagal reflexes which potentiate hypotension. Sufficient analgesia should be given to alleviate pain completely.

Digitalis Glycosides

There is considerable controversy concerning the role of digitalis glycosides in the syndrome of cardiogenic shock. The argument usually cited by physicians who are reluctant to utilize digitalis is the recognized potential of digitalis to cause ventricular arrhythmias. More recently, it has been shown that any intervention which increases the velocity of myocardial contraction also increases myocardial oxygen consumption. One of the actions of digitalis is to raise the velocity of contraction and therefore it may raise myocardial oxygen consumption. It has been demonstrated that areas of myocardium which are marginally oxygenated following an occlusion of a coronary artery may become necrotic instead of ischemic if myocardial oxygen consumption is augmented. However, if one accepts the thesis that the primary abnormality in cardiogenic shock is a marked depression of left ventricular contractility, then digitalis therapy becomes a very rational means of trying to restore circulatory integrity. Unfortunately a controlled study of digitalis therapy in cardiogenic shock is still not available.

It is the author's practice to administer digitalis early in the course of cardiogenic shock if the patient is not already taking this medication. The onset of action and peak effect of intravenous digoxin are such as to make it a perfectly reasonable drug to use. Between 1.0 and 1.5 mg of digoxin is given intravenously in approximately a two-hour period in doses of 0.25 mg every 15 or 20 minutes.

It should be noted that pulmonary venous congestion or other signs of left heart failure need not be present in a patient with cardiogenic shock. The author feels, nonetheless, that digitalis plays a role in the therapy of the patient in cardiogenic shock. It should be recognized, however, that this form of therapy is not agreed upon uniformly.

Vasopressors

The most easily recognizable feature of cardiogenic shock is hypotension. A variety of agents are available to raise arterial blood pressure. The sympathomimetic amines have been given considerable use. These drugs have been classified into alpha or beta stimulatory agents. Alpha adrenergic drugs act primarily on the peripheral arterioles and raise blood pressure by increasing peripheral resistance. Included in this group are methoxamine (Vasoxyl) and phenylephrine (Neo-synephrine). A second category of drug not only stimulates alpha adrenergic receptors in the peripheral arterioles but also stimulates beta adrenergic receptors in the myocardium. Metaraminol (Aramine®), nor-epinephrine (Levophed®) and epinephrine are examples of this type of agent. An example of a sympathomimetic amine which has only beta stimulating effects is isoproterenol (Isuprel®). Since isoproterenol acts as a peripheral vasodilator it does not appropriately fall into the category of a vasopressor, although it is a sympathomimetic amine.

Although raising the blood pressure is generally considered an appropriate goal in the treatment of a patient in cardiogenic shock, the issue is not quite that simple. Since most filling of the coronary arteries occurs in diastole, the coronary arteries do require a certain level of pressure in the central aorta in order to fill. Myocardial function is dependent upon adequate coronary blood-flow and will deteriorate in the presence of inadequate perfusion pressure.

It has been shown, however, that drugs which act only on the peripheral arterioles, thereby raising blood pressure by elevating peripheral vascular resistance, may have a deleterious effect upon patients in cardiogenic shock. If left ventricular function is sufficiently impaired to place a patient into cardiogenic shock, increasing the resistance against which the left ventricle must pump may further decrease cardiac output.

For this reason, drugs which act solely on the peripheral vasculature, such as methoxamine or phenylephrine, have little or no role in the therapy of cardiogenic shock.

Agents which act both on the beta receptors of the myocardium and the alpha receptors of the periphery have been used most extensively. It is wise to use no more of these agents than is necessary to maintain an adequate perfusion pressure and it is also advisable to give them by intravenous drip rather than intramuscularly, for blood pressure then can be titrated more precisely. It is not necessary for the blood pressure to be brought to normal levels. A systolic blood pressure of 90 to 100 mm of mercury is usually adequate. It is the author's practice to place 50 mg of metaraminol in 500 ml of 5 percent dextrose in water. This is infused at a rate sufficient to elevate blood pressure the desired amount.

Nor-epinephrine (Levophed) is another sympathomimetic amine which has potent effects upon both the peripheral and the central circulation. Although blood pressure can generally be raised by an intravenous drip of nor-epinephrine, experience indicates that relatively few patients survive if it becomes necessary to use this drug in order to sustain blood pressure.

Glucagon

Glucagon, a hormone which has been shown to raise blood sugar has also been utilized recently in patients with cardiogenic shock. Although its mechanism of action is not known precisely, it does have the property of increasing cardiac contractility, possibly by augmenting the synthesis of cyclic AMP. Initial studies of this agent in the animal laboratory and in the human cardiac catheterization laboratory led to some enthusiasm for its use in patients with myocardial infarction and shock. Other than for some anecdotal reports of its efficacy, this agent has generally been disappointing in the treatment of this condition and has generally been abandoned as a therapeutic agent.